A Microfluidic Pancreas-on-a-Chip Platform

Molecular and Functional Assessment of Gemcitabine–5FU Combination Therapy

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The Challenge in Pancreas Cancer Drug Development

Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal cancers. While **gemcitabine** remains a frontline therapy, most tumors display intrinsic resistance. Combination therapies, particularly with 5-fluorouracil (5-FU), are explored to overcome these limitations by targeting complementary molecular pathways.

Conventional preclinical models fall short:

- **2D cultures** lack tumor–stroma and vascular interactions
- **Animal models** poorly predict human drug response
- **Static assays** miss dynamic exposure and biomarker output

Our Solution: Pancreas cancer-on-a-Chip

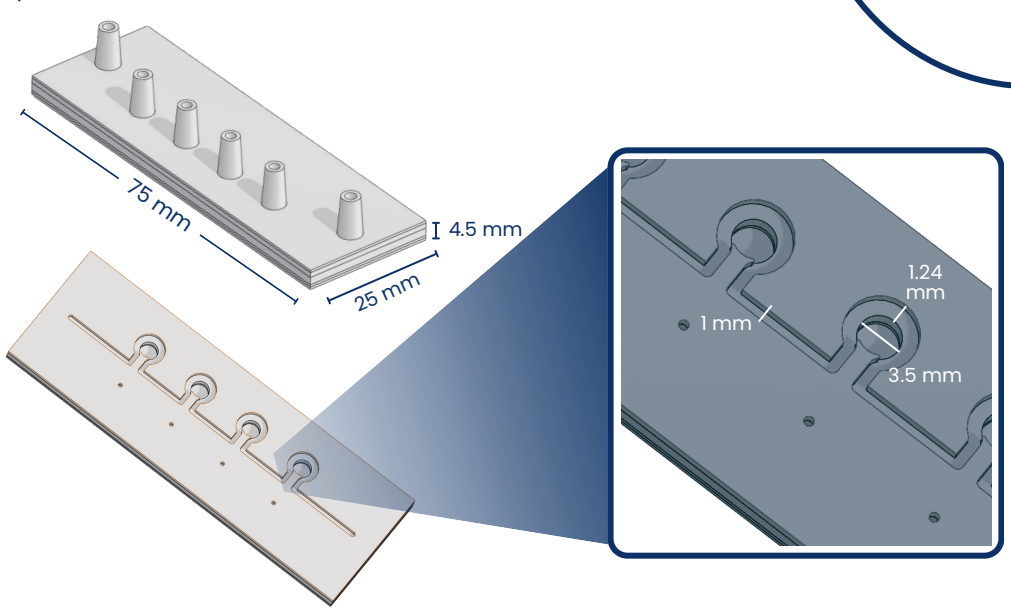
CanChip developed a 3D microfluidic cancer-on-a-chip model using **BxPC-3 pancreatic ductal adenocarcinoma cells**, a clinically relevant **gemcitabine-resistant PDAC model**.

Cultured under continuous perfusion, the system enables predictive evaluation of gemcitabine-based and combination therapies under physiologically relevant conditions.

- Maintains clinically relevant resistance phenotypes
- Provides physiological, flow-based drug exposure
- Enables quantitative molecular and functional analysis
- Ensures reproducibility via ISO 9001–aligned workflows

Chip Design

Chip Size:75mm×25mm×4.5 mm



Experimental Design

Phase I: Gemcitabine Monotherapy

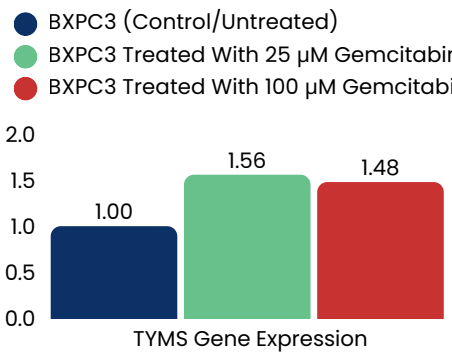
BxPC-3 cells were reseeded onto the microfluidic chip and divided into 3 groups, treated with Gemcitabine (25 and 100 µM)

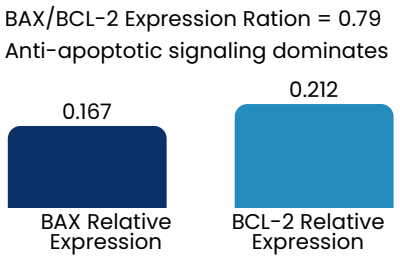
Gene Expression Analysis

- Analyzed the BAX/BCL-2 apoptosis ratio
- Measured CDKN1A, TOP2A, and TYMS expression levels

Results

- CDKN1A, TOP2A, and TYMS remained unchanged
- BCL-2 upregulation outweighed a modest BAX increase
- BAX/BCL-2 ratio decreased, an anti-apoptotic shift
- Confirms intrinsic gemcitabine resistance in BxPC-3 cells





Phase II: Combination Therapy with 5-FU and Gemcitabine

BxPC-3 cells were reseeded onto the microfluidic chip and divided into 3 groups, treated with Gemcitabine (50 and 100 µM) combines with 5-FU (50 µM)

Results

TYMS gene expression analysis

- Dose-dependent TYMS suppression with 5-FU + gemcitabine
- TYMS reduced to ~0.6-fold (50/50) and ~0.4-fold (50/100)
- The effect was highly reproducible across experiments
- Indicates sensitization of gemcitabine-resistant BxPC-3 cells

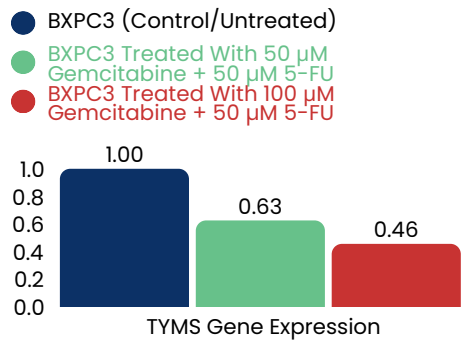
Positive Control Validation

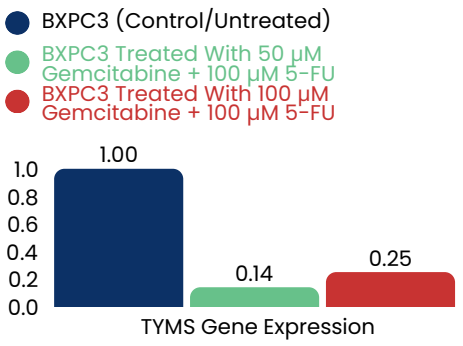
- High-dose 5-FU + gemcitabine used as positive controls
- TYMS expression reduced to ~0.1–0.2-fold
- Confirms platform sensitivity and responsiveness
- Validates combination therapy efficacy at higher doses

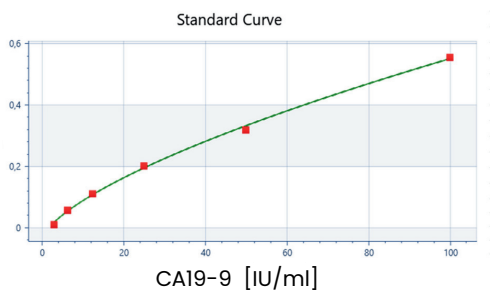
CA19-9 Secretion Analysis

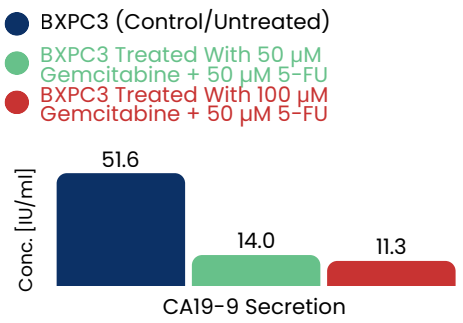
CA19-9 secretion quantified by ELISA after 24-hour treatment

- Assay showed high linearity (R^2 = 0.99)
- CA19-9 normalized for flow (10 mL total volume)
- Total CA19-9 output reduced from 516 IU (control) to 140 IU (50/50) and 113 IU (50/100)
- Confirms functional response consistent with molecular inhibition









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